B1 neuropeptide Y (NPY) and pancreatic polypeptide (PP). The sequence for human PYY is given by YPIKPEAPGEDASPEELNRYYASLRHYLNLVTRQRY (SEQ ID No: 2).

The replacement paragraph presented above incorporates changes as indicated by the marked-up version below.

PYY is the predominant hormone of the pancreatic polypeptide family in developing mouse and rat pancreas. It is a member of the PP family of proteins, which also includes neuropeptide Y (NPY) and pancreatic polypeptide (PP). The sequence for human PYY is given by YPIKPEAPGEDASPEELNRYYASLRHYLNLVTRQRY (SEQ ID No: ~~1~~2).

IN THE CLAIMS:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. A method for promoting the growth of pancreatic cells comprising contacting pancreatic cells with a composition including peptide YY (PYY) or an agonist thereof.

2. A method for reducing degeneration of pancreatic tissue comprising contacting the tissue with a composition including peptide YY (PYY) or an agonist thereof.

3. The method of claim 1 or 2, wherein the pancreatic cells or tissue include exocrine cells.

4. The method of claim 1 or 2, wherein the pancreatic cells or tissue include endocrine cells.

5. The method of claim 1 or 2, wherein the pancreatic cells or tissue include α, β, δ, or φ-cells.

6. The method of claim 2, wherein the pancreatic tissue includes insulin-producing islets.

7. **(Amended)** The method of claim 1 or 2, which utilizes a PYY peptide identical or homologous to SEQ ID No. 2, or an active fragment thereof.

8. The method of claim 1 or 2, which utilizes a PYY peptidomimetic.

9. **(Amended)** The method of claim 8, wherein the PYY peptidomimetic is a peptide homologous to SEQ ID No. 2, having one or amide bonds replaced with protease-resistant bonds, the peptidomimetic having a serum half-life longer than the peptide represented in SEQ ID No. 2.

10. The method of claim 1 or 2, which utilizes a non-peptidyl PYY agonist.

11. The method of claim 10, wherein the PYY agonist is a small organic molecule.

12. The method of claim 10, wherein the PYY agonist is a DPIV inhibitor.

13. A method for altering the differentiated state of a pancreatic islet or cell, comprising administering to the pancreatic islet or cell a PYY Therapeutic.

14. The method of claim 13, wherein administration of a PYY Therapeutic causes the islet or cell to be glucose responsive.

15. The method of claim 14, wherein said glucose responsive islet or cell produces insulin when treated with glucose.

16. The method of claim 13, wherein the islet is a fetal islet.

17. The method of claim 13, wherein the cell is a fetal pancreatic cell.

18. The method of claim 13, wherein the islet is a postpartem islet.

19. The method of claim 13, wherein the cell is a postpartem cell.

20. The method of claim 13, 17 or 19, wherein the cell is a pancreatic β cell.

21. A method for modifying glucose metabolism in an animal, comprising administering to the animal a pharmaceutically effective amount of a composition including a PYY Therapeutic.

22. The method of claim 21, wherein said PYY Therapeutic induces or enhances the glucose responsiveness of a pancreatic islet or cell.

23. A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal a pharmaceutically effective amount of a composition comprising a PYY Therapeutic, in an amount sufficient to increase the glucose responsiveness of a pancreatic islet or cell.

24. A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal a pharmaceutically effective amount of a composition comprising an antagonist of a PYY antagonist in an amount sufficient to increase the glucose responsiveness of a pancreatic islet or cell.

25. A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal a pharmaceutically effective amount of a composition comprising the glucose responsive islets or cells of claim 13, 14, 15, 17, 19 or 20.

26. The method of claim 25, wherein said composition further comprises a PYY Therapeutic.

27. The method of claim 26, wherein said composition is conjointly administered either simultaneously, sequentially or separately with a PYY Therapeutic.

28. The method of claim 23, 24 or 25, wherein said disease is associated with a condition selected from the group consisting of insulin resistance, glucose intolerance or glucose non-responsiveness, hyperglycemia, obesity, hyperlipidemia and hyperlipoproteinemia in a subject.

29. The method of claim 23, 24 or 24, wherein said disease is Type II diabetes mellitus (NIDD).

30. The method of any one of the claims 13-29, wherein said composition further comprises a dipeptidylpeptidase inhibitor, insulin or GLP-1.

31. The method of any one of claims 13-29, wherein said composition is conjointly administered either simultaneously, sequentially or separately with a dipeptidylpeptidase inhibitor, insulin or GLP-1.

32. The method of claim 30 or 31, wherein said dipeptidylpeptidase is DPIV.

33. A method for obtaining functional pancreatic β cells, comprising administering to a pancreatic islet or cell a composition comprising a PYY Therapeutic.

34. The method of any one of claims 13-33, wherein said agonist is a small organic molecule.

35. The method of any one of claims 13-33, wherein said composition further comprises an agent capable of inhibiting the degradation of a PYY Therapeutic.

36. The method of any one of claims 13-33, further comprising the step of administering to an animal an agent capable of inhibiting the degradation of a PYY Therapeutic either simultaneously, sequentially or separately with said PYY or a PYY agonist.

37. The method of claim 34, wherein said agent is co-administered with the PYY Therapeutic.

38. A method for identifying a PYY homolog, PYY analog, PYY agonist, PYY antagonist or an antagonist to a PYY antagonist, comprising administering to a pancreatic islet or cell an effective amount of an agent and comparing the cellular response to the agent to the cellular response to PYY or agonist.

39. The method of any of claims 13-38, wherein said PYY Therapeutic enhances or recovers glucose responsiveness.

40. A method for screening a DNA library for the presence of a PYY homolog, PYY analog, PYY agonist, PYY antagonist or an antagonist to a PYY antagonist.

41. A method for identifying antagonists of PYY, comprising administering an agent to a pancreatic islet or cell and determining the glucose-responsiveness as compared to cells not treated with an agent.

42. The method of claim 39, wherein the antagonist is naturally occurring.

43. The method of claim 39, wherein the antagonist is synthetic.

44. The method of claim 41-43, wherein said antagonist is selected from the group consisting of an antisense, a ribozyme molecule and a small organic molecule.

45. A method for maintaining normal pancreatic islet function, comprising administering to a cultured pancreatic islet or cell a PYY Therapeutic.

46. The method of claim 45, where in said pancreatic islet is a failing β cell.

47. A functionally mature islet or β cell generated in cell culture by contacting undifferentiated cells from an animal with a PYY Therapeutic.

48. A composition suitable for pharmaceutical administration comprising

(i) at least one polypeptide capable of functioning in one of either role of an agonist of at least one biological activity of a vertebrate PYY protein or an antagonist of at least one biological activity of said vertebrate PYY protein; and

(ii) a pharmaceutically acceptable carrier,

wherein said composition induces glucose responsiveness in pancreatic islet or cells.

49. A transgenic non-human animal in which PYY inductive pathways are inhibited in one or more tissue of said animal by one of either expression of an antagonistic PYY polypeptide or disruption of a gene encoding a PYY Therapeutic.

50. The method of any one of the above claims 13-49, wherein said animal is a human.

The amended claims are re-stated below to reflect changes with respect to the last filing.

7. The method of claim 1 or 2, which utilizes a PYY peptide identical or homologous to SEQ ID No. ~~1~~2, or an active fragment thereof.

9. The method of claim 8, wherein the PYY peptidomimetic is a peptide homologous to SEQ ID No. ~~1~~2, having one or amide bonds replaced with protease-resistant bonds, the peptidomimetic having a serum half-life longer than the peptide represented in SEQ ID No. ~~1~~2.

Although Applicants believe no fees are due, the Commissioner is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit

Account No. 18-1945, under Order No. CIBT-P02-058. Please direct any questions arising from this submission to the undersigned at (617) 951-7615.

Respectfully Submitted,

Date: November 18, 2002

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